SYNTHESIS OF SOME EPITESTOSTERONE ANALOGUES*

Hana CHODOUNSKA, Barbora SLAVIKOVA and Alexander KASAL

Institute of Organic Chemistry and Biochemistry,
Academy of Sciences of the Czech Republic, 166 10 Prague 6, The Czech Republic

Received April 2, 1993
Accepted April 20, 1993

11β-Hydroxyandrost-4-ene-3,17-dione (*III*) was converted into a potential metabolite of epitestosterone – 11β,17α-dihydroxyandrost-4-en-3-one (*II*) in 5 steps, including the inversion of configuration of a 17β-hydroxy group. This inversion was not feasible in the preparation of the analogues *X*, *XIV*, *XX*, and *XXII*, where the 17α-hydroxy group was introduced first and only then was the rest of the molecule modified.

Recently[1] we published the preparation of several metabolites of epitestosterone (17α-hydroxyandrost-4-en-3-one, *I*) needed for metabolic studies of epitestosterone in man. Now we report on the synthesis of another potential epitestosterone metabolite and of other analogues which may exert some of its biological properties.

One of the epitestosterone's potential metabolites is the product of its 11β-hydroxylation, compound *II*. Lindner[2] prepared this compound once by the enzymatic reduction of 11β-hydroxyandrost-4-ene-3,17-dione (*III*) without, however, precisely characterizing it.

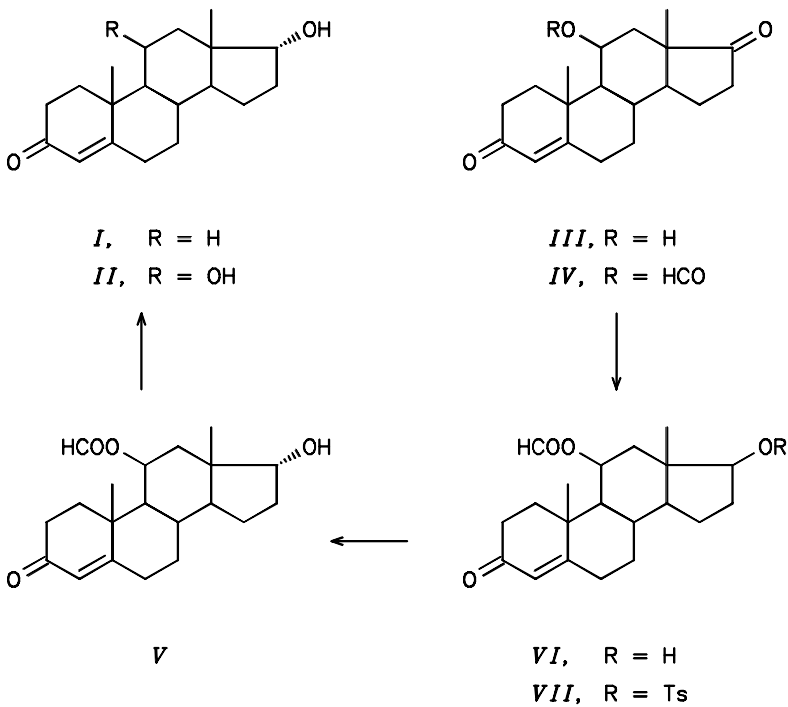
Commercially available 11β-hydroxyandrost-4-ene-3,17-dione (*III*) was esterified to formate *IV* which was then subjected to partial reduction[3] of the 17-oxo group by tri-*tert*-butoxy lithium aluminium hydride (see Scheme 1). In the thus formed 17β-alcohol *VI*, inversion of the configuration of the 17-hydroxy group was carried out according to Lattrell and Lohaus[4], i.e., by solvolysis of the corresponding tosylate *VII* with sodium nitrite in dimethyl sulfoxide. The expected 17α-alcohol *V* was isolated from the mixture and identified according to its spectral properties (see Experimental). The low yield (6%) could not be increased using more moderate conditions: lipophilic by-products were formed even in temperatures under which the tosyloxy group survived un-

* Part CCCLXXII in the series On Steroids; Part CCCLXXI: Collect. Czech. Chem. Commun. *58*, 3000 (1993).

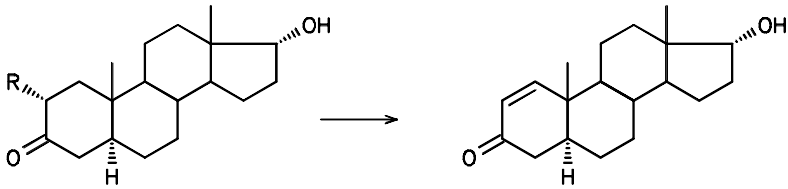
changed. For this reason in other experiments the 17α-hydroxy group was introduced first and then the sensitive A ring modified.

One of the analogues with potential antiandrogenic activity was the epitestosterone isomer *X*, containing a 1(2)-double bond, which in some cases increased the 5α-reductase inhibitory activity (see, e.g., ref.[5]). Compound *X* was once prepared from 17β-hydroxyandrost-1-en-3-one[6], but we synthesized (Scheme 2) this compound in 78% yield from dihydroepitestosterone (*VIII*, 17α-hydroxy-5α-androstan-3-one[1,7]); ketone *VIII* was brominated by phenyltrimethylammonium tribromide[8] and the formed 2α-bromo ketone[9] *IX* was dehydrobrominated by adding it to a boiling solution of lithium salts in *N*,*N*-dimethylformamide.

Briefly we report on the preparation of two epitestosterone homologues, the synthesis of which has already been described, in order to supply additional data and comment on a modification of the procedure. The first is 17α-hydroxy-17β-methylandrost-4-en-3-one (*XIV*), prepared by Miescher[10] from diol *XII*. Compound *XII* is a lipophilic



SCHEME 1

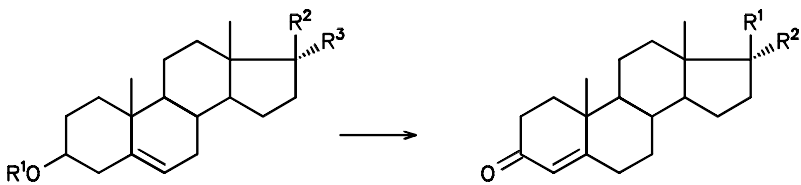


VIII, R = H
IX, R = Br

X

SCHEME 2

admixture in the product of the reaction of 17-ketone *XI* with methylmagnesium iodide. We found that the purity of both diol *XII* and hydroxy ketone *XIV* could easily be checked by ^{1}H NMR spectroscopy: chemical shift of H-18 protons appears at significantly higher field in the 17α-hydroxy derivatives *XII* and *XIV* than in the corresponding 17β-isomers *XIII* and *XV*, respectively.

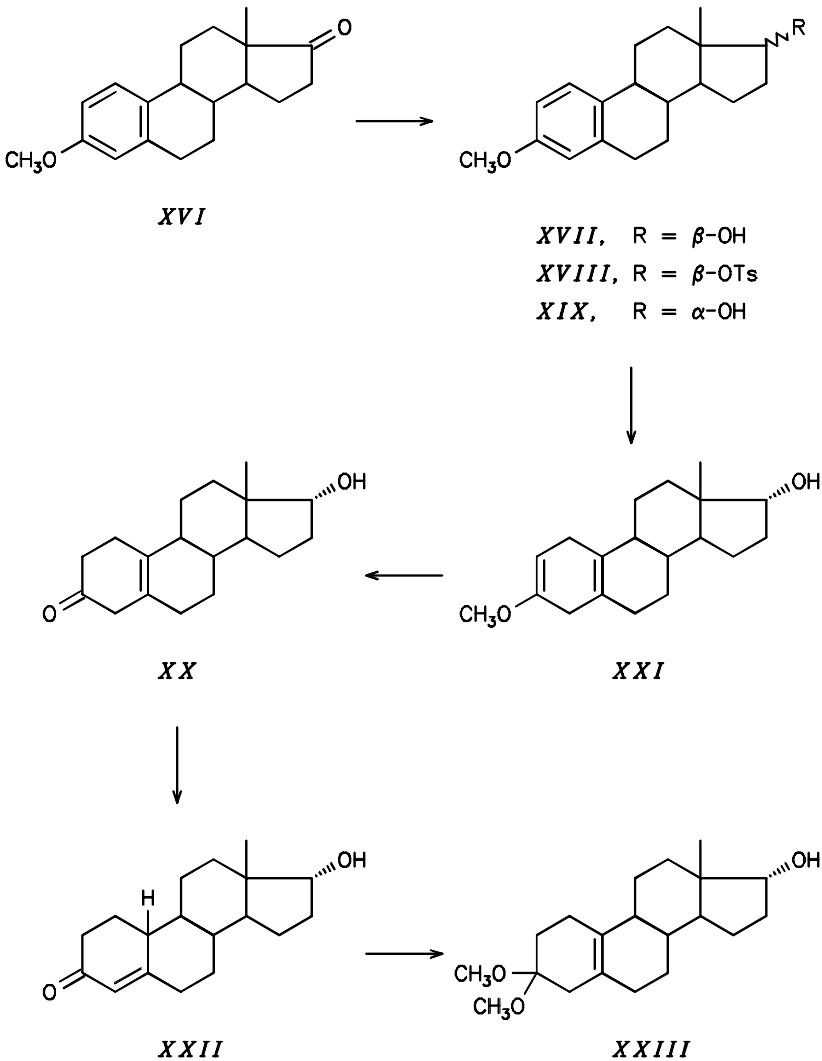


XI, R^1 = Ac; $R^2 + R^3$ = O
XII, R^1 = H; R^2 = CH_3; R^3 = OH
XIII, R^1 = H; R^2 = OH; R^3 = CH_3

XIV, R^1 = CH_3; R^2 = OH
XV, R^1 = OH; R^2 = CH_3

The second homologue, 19-nor-epitestosterone (*XXII*, ref.[11]) is the major metabolite of nandrolone (i.e. an anabolic steroid applied in fodder) and its residue in meat had to be monitored (see, e.g., ref.[12]). We prepared (see Scheme 3) this compound from estrone methyl ether (*XVI*) via 3-methoxy-1,3,5(10)-estratrien-17α-ol[13 – 15] (*XIX*). The aromatic system of compound *XIX* was reduced[16] by lithium in ammonia, using tetrahydrofuran and 2-methyl-2-propanol as a solvent. The already described[11] cleavage of the enol ether *XXI* by a methanolic solution of oxalic acid yielded a mixture of the hydroxy ketones *XX* and *XXII*. The same reagent with a lower concentration of acid[17] gave rise mainly to the 3,3-dimethoxy derivative *XXIII*. It turned out that the best method for the

conversion of *XXI* to 5(10)-unsaturated ketone *XX* was treatment with wet silica gel, and for the conversion to the unsaturated ketone *XXII* was treatment with hydrochloric acid.



XVI

XVII, R = β-OH
XVIII, R = β-OTs
XIX, R = α-OH

XX *XXI*

XXII *XXIII*

SCHEME 3

The results of biochemical and biological experiments with compounds prepared above will be discussed later.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer PE 580 spectrometer in chloroform, wavenumbers are given in cm^{-1}. Proton NMR spectra were taken in deuteriochloroform on an XL-200 (FT mode, 200 MHz) Varian instrument with tetramethylsilane as the internal reference. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) and multiplet width (*W*) in Hz. The data were interpreted as the first-order spectra. The identity of the prepared samples was checked by mixture melting point determination, thin-layer chromatography (TLC), IR and proton NMR spectra. Preparative TLC was carried out on 200 × 200 mm plates coated with 0.7 mm thick layer of Woelm DC silica gel. The light petroleum was a fraction boiling at 40 – 62 °C.

3,17-Dioxo-4-androsten-11β-yl Formate[3] (*IV*)

^{1}H NMR spectrum: 8.09 s, 1 H (OCOH); 5.71 d, 1 H (H-4, $J(4,6) \approx 1$); 5.64 q, 1 H (H-11α, $J(11\alpha,12\alpha) \approx J(11\alpha,12\beta) \approx J(11\alpha,9\alpha) \approx 2.5$); 1.33 s, 3 H (3 × H-19); 1.06 s, 3 H (3 × H-18).

17β-Hydroxy-3-oxo-4-androsten-11β-yl Formate[3] (*VI*)

^{1}H NMR spectrum: 8.10 s, 1 H (OCOH); 5.71 d, 1 H (H-4, $J(4,6) \approx 1$); 5.56 q, 1 H (H-11α, $J(11\alpha,12\alpha) \approx J(11\alpha,12\beta) \approx J(11\alpha,9\alpha) \approx 2.5$); 3.61 dd, 1 H (H-17α, $J(16\beta,17\alpha) = 7.5$, $J(16\alpha,17\alpha) = 8.5$).

3-Oxo-4-androstene-11β,17β-diyl 11-Formate 17-Tosylate (*VII*)

p-Toluenesulfonyl chloride (2.0 g, 10.5 mmol) was added to a solution of *VI* (1.6 g, 5.0 mmol) in pyridine (30 ml) cooled with an ice bath. This mixture was allowed to stand overnight at 40 °C. Then it was poured onto ice, extracted with ethyl acetate, the organic layer was washed with 5% hydrochloric acid, water, 5% aqueous sodium hydrogen carbonate and dried over anhydrous magnesium sulfate. Evaporation of the solvent in vacuo afforded 2.1 g (86%) of crude product *VII*, which resisted all attempts at crystallization, even after preparative chromatography on a thin layer of silica gel, in toluene–ether (1 : 1); $[\alpha]_D$ +53° (*c* 0.9, chloroform). IR spectrum: 1 718 (C=O, formate); 1 666 (C=O, ketone); 1 617 (C=C); 1 168 shoulder (C–O, formate); 1 362, 1 176 (SO2); 1 097, 1 020 (C–O). ^{1}H NMR spectrum: 8.43 s, 1 H (OCOH); 7.75 d, 2 H (H-2′ and H-6′ tosylate, $J = 8.5$); 7.33 d, 2 H (H-3′ and H-5′, tosylate, $J = 8.5$); 5.68 d, 1 H (H-4, $J(4,6) \approx 1$); 5.46 q, 1 H (H-11α, $J(11\alpha,12\alpha) \approx J(11\alpha,12\beta) \approx J(11\alpha,9\alpha) \approx 2.5$); 4.22 dd, 1 H (H-17α, $J(16\beta,17\alpha) = 7.5$, $J(16\alpha,17\alpha) = 8.5$); 2.45 s, 3 H ($CH_3$, tosylate); 1.28 s, 3 H (3 × H-19); 0.97 s, 3 H (3 × H-18). For $C_{27}H_{34}SO_6$ (468.6) calculated 66.64% C, 7.04% H, 6.59% S; found: 66.61% C, 7.11% H, 6.47% S.

17α-Hydroxy-3-oxo-4-androsten-11β-yl Formate (*V*)

A mixture of *VII* (2.0 g, 4.1 mmol) and sodium nitrite (2.5 g, 36 mmol) in dimethyl sulfoxide (70 ml) was stirred at 150 °C for 2 h. The mixture was cooled at room temperature, diluted with water (200 ml) and extracted with ether (3×). The combined organic layers were washed with water (5×), dried over anhydrous magnesium sulfate, and the solvent was evaporated in vacuo. Chromatography of the residue (1.8 g) on a column of Silpearl (100 g) in toluene–ether (1 : 1) and then on the thin layer of silica gel in toluene–ether–methanol (140 : 140 : 1) afforded 80 mg (6%) of *V*, m.p. 209 – 211 °C (methanol), $[\alpha]_D$ +150° (*c* 0.4, chloroform). IR spectrum: 3 619, 3 435, 3 309 (OH); 1 717 (C=O, formate); 1 662 (C=O, ketone); 1 618 (C=C); 1 193, 1 178 (C–O, formate); 1 057 (C–O, 17-OH); 868 (=C–H). ^{1}H NMR spectrum: 8.40 s, 1 H (OCOH); 5.70 d , 1 H (H-4, $J(4,6) \approx 1$); 5.64 q, 1 H (H-11α, $J(11\alpha,12\alpha) \approx J(11\alpha,12\beta) \approx J(11\alpha,9\alpha) \approx 2.5$); 3.73 d, 1 H (H-17β, $J \approx 6$); 1.31 s, 3 H

(3 × H-19); 0.84 s, 3 H (3 × H-18). For $C_{20}H_{28}O_4$ (332.4) calculated: 72.26% C, 8.49% H; found: 72.11% C, 8.43% H.

11β,17α-Dihydroxy-4-androsten-3-one (*II*)

Sodium methoxide in methanol (5%, 30 drops) was added to a solution of *V* (40 mg, 0.12 mmol) in methanol (25 ml) and the mixture was stirred at 60 °C. After 8 h the reaction mixture was neutralized with solid carbon dioxide (about 400 mg) and the solvent was evaporated in vacuo. Chromatography of the residue on a thin layer of silica gel in toluene–ether–methanol (15 : 9 : 1) gave 32 mg (88%) of *II*, m.p. 207 – 209 °C (methanol–ether); $[\alpha]_D$ +114° (*c* 0.1, methanol–chloroform, 1 : 1). IR spectrum: 3 617, 3 460 (OH); 1 660 (C=O); 1 616 (C=C); 1 072, 1 053, 1 030, 1 020 (C–O); 867 (=C–H). ^{1}H NMR spectrum: 5.64 d, 1 H (H-4, $J(4,6) \approx 1$); 4.44 q, 1 H (H-11α, $J(11\alpha,12\alpha) \approx J(11\alpha,12\beta) \approx J(11\alpha,9\alpha) \approx 2.5$); 3.67 d, 1 H (H-17β, $J \approx 6$); 1.45 s, 3 H (3 × H-19); 0.95 s, 3 H (3 × H-18). For $C_{19}H_{28}O_3$ (304.4) calculated: 74.96% C, 9.27% H; found: 74.87% C, 9.30% H.

2α-Bromo-17α-hydroxy-5α-androstan-3-one (*IX*)

Phenyltrimethylammonium tribromide[8] (233 mg, 0.62 mmol) was added to a solution of ketone[1] *VIII* (150 mg, 0.52 mmol) in tetrahydrofuran (3 ml). The reaction mixture turned turbid immediately and a white precipitate was formed. The mixture was poured into a saturated aqueous solution of potassium hydrogen carbonate and the product was extracted with ether. The organic layer was washed with a saturated aqueous solution of potassium hydrogen carbonate, and water and dried over anhydrous sodium sulfate. Evaporation of the solvent in vacuo yielded 179 mg (94%) of crude *IX*, which was used in the next step without purification. A sample for analysis was crystallized from ether–heptane, m.p. 128 – 132 °C; $[\alpha]_D$ +9° (*c* 1.5, chloroform). ^{1}H NMR spectrum: 4.75 dd, 1 H (H-2β, $J(2\beta,1\beta) = 6.4$, $J(2\beta,1\alpha) = 13.4$); 3.75 d, 1 H (H-17β, $J = 5.8$); 1.10 s, 3 H (3 × H-19); 0.68 s, 3 H (3 × H-18).

17α-Hydroxy-5α-androst-1-en-3-one (*X*)

A solution of the bromo ketone *IX* (179 mg, 0.5 mmol) in *N,N*-dimethylformamide (3 ml) was added dropwise to a suspension of lithium carbonate (193 mg, 2.6 mmol) and lithium bromide (223 mg, 2.6 mmol) in boiling *N,N*-dimethylformamide (3.5 ml). After 1 h the mixture was cooled, diluted with ether, washed with a saturated aqueous solution of sodium chloride, and dried over anhydrous sodium sulfate. The solvent was evaporated in vacuo. Preparative chromatography on a thin layer of silica gel, (elution with benzene–ether, 1 : 1) afforded 117 mg (83%) of *X*: m.p. 116 – 118 °C (ether–heptane); $[\alpha]_D$ +30° (*c* 1.5, chloroform); the literature[6] gives m.p. 120 °C. ^{1}H NMR spectrum: 7.18 d, 1 H (H-1, $J = 10.4$); 5.86 bd, 1 H (H-2, $J = 10.4$); 3.76 d, 1 H (H-17β, $J = 6$); 1.02 s, 3 H (3 × H-19); 0.70 s, 3 H (3 × H-18).

17α-Hydroxy-17β-methylandrost-5-en-3β-ol (*XII*)

Compound *XII* was isolated[10] from the mother liquors of *XIII* (see the following experiment) as the more lipophilic admixture. ^{1}H NMR spectrum: 5.36 d, 1 H (H-6, $J \approx 5.2$); 3.53 m, 1 H (H-3, $W \approx 35$); 1.20 s, 3 H (CH_3-17β); 1.03 s, 3 H (3 × H-19); 0.70 s, 3 H (3 × H-18).

17β-Hydroxy-17α-methylandrost-5-en-3β-ol (*XIII*)

Compound *XIII* was prepared[18] from the 17-oxoandrost-5-en-3β-yl acetate by reacting it with methylmagnesium iodide, the only difference being the solvent: ether was later replaced by benzene. The

precipitate formed consisted of compound *XIII*. ^{1}H NMR spectrum: 5.35 d, 1 H (H-6, $J \approx 5.2$); 3.52 m, 1 H (H-3, $W \approx 36$); 1.21 s, 3 H (CH_3-17α); 1.03 s, 3 H (3 × H-19); 0.87 s, 3 H (3 × H-18).

17α-Hydroxy-17β-methylandrost-4-en-3-one (*XIV*)

The derivative *XIV* was prepared[10] by Oppenauer oxidation of compound *XII*. ^{1}H NMR spectrum: 5.73 d, 1 H (H-4, $J \approx 1.7$); 1.21 s, 3 H (CH_3-17β); 1.20 s, 3 H (3 × H-19); 0.73 s, 3 H (3 × H-18).

17β-Hydroxy-17α-methylandrost-4-en-3-one[18] (*XV*)

^{1}H NMR spectrum: 5.73 d, 1 H (H-4, $J = 1.5$); 1.22 s, 3 H (CH_3-17α); 1.21 s, 3 H (3 × H-19); 0.91 s, 3 H (3 × H-18).

3-Methoxy-1,3,5(10)-estratrien-17α-ol (*XIX*)

Sodium nitrite (12.0 g, 17.0 mmol) was added to a solution of the tosylate *XVIII* (4.0 g, 9.0 mmol), prepared[14] from compound *XVII*) in *N*,*N*-dimethylformamide (170 ml) and the mixture was stirred at 145 °C for 4 h. After cooling it was poured into a mixture of ether (500 ml) and water (500 ml), the aqueous layer was extracted with ethyl acetate (300 ml) and the combined organic phases were washed with water (2×). The solvents were evaporated and the residue (4 g) chromatographed on a column of Silpearl (200 g). Elution with light petroleum–ether (3 : 1) removed the non-polar side products (1.0 g, 50%), elution with light petroleum–ether (1 : 1) afforded compound *XIX* (1.3 g), m.p. 112 – 114 °C (hexane–ether); $[\alpha]_D$ +58° (*c* 0.8, chloroform). The literature[14] gives m.p. 110 – 112 °C, $[\alpha]_D$ +59°. ^{1}H NMR spectrum: 7.22 d, 1 H (H-1, $J(1,2) = 8.5$); 6.71 dd, 1 H (H-2, $J(1,2) = 8.5$, $J(2,4) = 2.5$); 6.63 d, 1 H (H-4, $J(4,2) = 2.5$); 3.80 d, 1 H (H-17β, $J(17,16) = 6$); 3.78 s, 3 H (OCH_3); 2.85 m, 2 H (2 × H-6, $W = 24$); 0.70 s, 3 H (3 × H-18). For $C_{19}H_{26}O_2$ (286.4) calculated: 79.68% C; 9.15% H; found: 79.46% C, 9.24% H.

3-Methoxy-2,5(10)-estradien-17α-ol (*XXI*)

Lithium wire (0.3 g, 50 mmol) was added to a solution of *XIX* (1.0 g, 3.5 mmol) in a mixture of tetrahydrofuran (20 ml), 2-methyl-2-propanol (20 ml) and liquid ammonia (100 ml, distilled from sodium). After stirring under a dry ice condenser for 1/2 h, the ammonia was distilled off and the mixture was diluted with water and allowed to stand for 2 h. The mixture was then filtered, and the crude product (1 g) washed with water and dried on air. Filtration of the ethereal solution through silica gel (pretreated with ammonia vapours) and crystallization from ether–hexane gave 670 mg (68%) of *XXI*, m.p. 110 – 113 °C; $[\alpha]_D$ +96° (*c* 0.4, chloroform). Literature[10] gives m.p. 112 – 114 °C, $[\alpha]_D$ +99°. IR spectrum: 3 615, 3 471 (O–H); 2 827 (OCH_3); 1 695, 1 665 (C=C); 1 026 (C–O). ^{1}H NMR spectrum: 4.69 t, 1 H (H-2, $J = 2.9$); 3.62 d, 1 H (H-17β, $J = 5.8$); 3.50 s, 3 H (3 × H, OCH_3); 0.65 s, 3 H (3 × H-18). For $C_{19}H_{28}O_2$ (288.4) calculated: 79.12% C, 9.78% H; found: 79.32% C, 9.67% H.

17α-Hydroxyestr-5(10)-en-3-one (*XX*)

A mixture of *XXI* (200 mg, 0.7 mmol), silica gel (2 g), 2-methyl-2-propanol (0.5 ml), water (0.5 ml) and toluene (10 ml) was evaporated on a rotatory evaporator in vacuo for 15 min at 50 °C. Elution of the silica gel with ether and evaporation of the solvent in vacuo gave 160 mg (83%) of *XX*, m.p. 141 – 150 °C decomposition (ether–hexane), $[\alpha]_D$ +160° (*c* 0.5, chloroform). The literature[11] gives m.p. 144 – 150 °C, $[\alpha]_D$ +164°. IR spectrum: 3 616, 3 468 (OH); 1 712 (C=O); 1 434 (CH_2–C=O). ^{1}H NMR spectrum: 3.78 d, 1 H (H-17β, $J = 5.6$); 2.81 d, 1 H (H-4a, $J(4a,4b) \approx 22$); 2.67 d, 1 H

(H-4b, J(4a,4b) ≈ 22); 0.69 s, 3 H (3 × H-18). For $C_{18}H_{26}O_2$ (274.4) calculated: 78.79% C, 9.55% H; found: 78.79% C, 9.53% H.

3,3-Dimethoxyestr-5(10)-en-17α-ol (*XXIII*)

A solution of *XXI* (40 mg, 0.07 mmol) and oxalic acid dihydrate (5 mg, 0.05 mmol) in methanol (25 ml) was allowed to stand for 48 h at 5 °C. The reaction mixture was diluted with water (25 ml) and ether (25 ml) and the aqueous layer extracted with ether (20 ml, 3×). The combined organic layers were washed with an aqueous solution of sodium hydrogen carbonate (25 ml, 5%), dried over anhydrous magnesium sulfate and evaporated in vacuo. The residue was chromatographed on a thin layer of silica gel in light petroleum–ether (1 : 1), affording 36 mg (80%) of product *XXIII*, m.p. 86 – 88 °C (ether–hexane), $[\alpha]_D$ +128° (*c* 0.7, chloroform). IR spectrum: 3 615, 3 471 (O–H); 2 832 (OCH_3); 1 167, 1 130, 1 090, 1 048 (C–O–C–O–C); 930 (OCH_3). ^{1}H NMR spectrum: 3.67 d, 2 H (H-17β, J = 6.5); 3.25 s, 3 H (OCH_3); 3.22 s, 3 H (OCH_3); 0.68 s, 3 H (3 × H-18). For $C_{20}H_{32}O_3$ (320.5) calculated: 74.96% C, 10.06% H; found: 75.18% C, 9.93% H.

17α-Hydroxyestr-4-en-3-one (*XXII*)

a) Hydrochloric acid (0.5 ml, 37%) was added to a solution of *XXI* (30 mg, 0.11 mmol) in chloroform (10 ml). The mixture was set aside for 1 h at room temperature, then it was washed with water (5 ml, 2×), a solution of sodium hydrogen carbonate (5 ml, 5%), and dried over anhydrous magnesium sulfate. Evaporation of the solvent and crystallization from ether–hexane gave 22 mg (73%) of *XXII*, m.p. 146 – 150 °C (decomposition); $[\alpha]_D$ +12° (*c* 1.7, chloroform). The literature[11] gives m.p. 146 – 149 °C; $[\alpha]_D$ +9°. IR spectrum: 3 617, 3 742 (O–H); 1 664 (C=O); 1 618 (C=C); 868 (=C–H). ^{1}H NMR spectrum: 5.84 t, 1 H (H-4, J(4,6) ≈ J(4,10) ≈ 1); 3.78 d, 1 H (H-17β, J = 5.6); 0.73 s, 3 H (3 × H-18). For $C_{18}H_{26}O_2$ (274.4) calculated: 78.79% C, 9.55% H; found: 78.64% C, 9.49% H.

b) A solution of oxalic acid dihydrate (220 mg, 2 mmol) in water (2 ml) was added to a solution of *XXI* (200 mg, 0.69 mmol) in methanol (20 ml). After standing for 1 h at room temperature the mixture was diluted with water (50 ml) and ether (50 ml) and the aqueous layer extracted with ether (3×). The combined organic layers were washed with an aqueous solution of sodium hydrogen carbonate (30 ml, 5%), dried over anhydrous magnesium sulfate and evaporated in vacuo. Chromatography of the crude product (178 mg) on a column of Silpearl (60 g), and elution with light petroleum–ether (1 : 1) gave 110 mg (58%) of *XX* and 40 mg (22%) of *XXII*.

The authors are indebted to the Analytical Laboratory (Dr V. Pechanec, Head) for the elemental analyses, the Laboratory of NMR Spectroscopy (Dr M. Budesinsky, Head) for measurement of ^{1}H NMR spectra, to Dr P. Fiedler and Dr J. Smolikova for the measurement and interpretation of IR spectra. The project was supported by a grant of the Czechoslovak Academy of Sciences (GA 45520).

REFERENCES

1. Kasal A., Fuksova K., Pouzar V.: Collect. Czech. Chem. Commun. *58*, 600 (1993).
2. Lindner H. R.: Steroids Suppl. *2*, 133 (1965).
3. Fajkos J., Joska J.: Collect. Czech. Chem. Commun. *45*, 1845 (1980).
4. Lattrell R., Lohaus G.: Justus Liebigs Ann. Chem. *1974*, 901.
5. Steinberg N. G., Rasmusson G. H., Gary H., Salzmann T. N.: Eur. Pat. Appl. EP 462,665; Chem. Abstr. *116*, 152148f (1992).
6. Braselton W. E., jr., Engel L. L., Orr J. C.: Eur. J. Biochem. *48*, 35 (1974).

7. Ruzicka L., Kagi H.: Helv. Chim. Acta *20*, 1557 (1937).
8. Marquet A., Dvolaitzky M., Kagan H. B., Mamlok L., Ouannes C., Jacques J.: Bull. Soc. Chim. Fr. *1961*, 1822.
9. Jones R. N., Ramsay D. A., Herling F., Dobriner K.: J. Am. Chem. Soc. *74*, 2828 (1952).
10. Miescher K., Klarer W.: Helv. Chim. Acta *22*, 962 (1939).
11. Robinson C. H., Gnoj O., Oliveto E. P.: J. Org. Chem. *25*, 2247 (1960).
12. van Look L. J., Jansen E. H. J. M., van den Berg R. H., Zomer G., Vanoosthuyze K. E., van Peteghem C. H.: J. Chromatogr. *564*, 451 (1991).
13. Kincl F. A., Ringold H. J., Rosenkranz G.: U.S. 2,906,758; Chem. Abstr. *54*, 3519f (1960).
14. Schneider G., Hackler L., Sohar P.: Liebigs Ann. Chem. *1988*, 679.
15. Fedorova O. I., Pekarskaya E. S., Lukachina I. V., Trinenko T. S.: Khim. Farm. Zh. *8*, 9 (1974).
16. Birch A. J., Smith H.: Rev. Chem. Soc. *12*, 17 (1958).
17. Ueberwasser H., Heusler K., Kalvoda J., Meystre Ch., Wieland P., Anner G., Wettstein A.: Helv. Chim. Acta *46*, 344 (1963).
18. Ruzicka L., Goldberg M. W., Rosenberg H. R.: Helv. Chim. Acta *18*, 1487 (1935).

Translation revised by J. Kovarova.